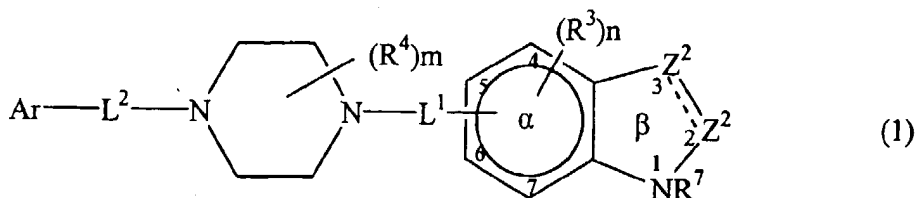


CLAIMS AMENDMENT

1. (currently amended): A compound of the formula:



and the pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof, wherein

\diagup represents a single or double bond;

one Z^2 is CA or CR^8A and the other is CR^1 , CR^1_2 , NR^6 or N_1

wherein each R^1 [~~R^6 and R^8~~] is independently hydrogen or ~~noninterfering substituent~~ is alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, NH-aroyl, halo, OR, NR_2 , SR, SOR , SO_2R , OCOR, NRCOR, $NRCONR_2$, $NRCOOR$, $OCONR_2$, RCO, COOR, alkyl-OOCR, SO_3R , $CONR_2$, SO_2NR_2 , $NRSO_2NR_2$, CN, CF_3 , R_3Si , and NO_2 , wherein each R is independently H, alkyl, alkenyl or aryl;

R^6 is H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, or heteroaryl, or is SOR , SO_2R , RCO, COOR, alkyl-COR, SO_3R , $CONR_2$, SO_2NR_2 , CN, CF_3 , or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl;

R^8 is H, halo, alkyl or alkenyl;

A is $-W_1-COXY$ wherein Y is COR^2 wherein R^2 is hydrogen or is straight or branched chain alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, or heteroarylalkyl, each optionally substituted with halo, alkyl, SR, OR, NR_2 , OCOR, NRCOR, $NRCONR_2$, $NRSO_2R$, $NRSO_2NR_2$, $OCONR_2$, CN, COOR, $CONR_2$, COR, or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl ~~or the forms thereof containing 1-2 O, S and/or N atoms~~, or

wherein R^2 is OR, NR_2 , $NRCONR_2$, $OCONR_2$, $NRSO_2NR_2$, heteroarylalkyl, COOR, $NRNR_2$, heteroaryl, heteroaryloxy, ~~heteroaryl- NR_2~~ heteroaryl-NR, or NROR wherein each R is independently H, alkyl, alkenyl or aryl ~~or the forms thereof containing 1-2 O, S and/or N atoms~~, and wherein two R attached to the same N atom may form a 3-8 member ring selected from the group consisting of a piperazine ring, a morpholine ring, a thiazolidine ring, an oxazolidine ring, a

pyrrolidine ring, a piperidine ring, an azacyclopropane ring, an azacyclobutane ring and an azacyclooctane ring; and wherein said ring may further be substituted by alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, each optionally substituted with halo, SR, OR, NR₂, OCOR, NRCOR, NRCONR₂, NRSO₂R, NRSO₂NR₂, OCONR₂, or R₃Si wherein each R is independently H, alkyl, alkenyl or aryl ~~or the forms thereof containing 1-2 O, S and/or N atoms~~ wherein two R attached to the same N atom may form a 3-8 member ring, optionally substituted as above defined, and

each of W and X is substituted or unsubstituted alkylene, alkenylene or alkynylene, each of 2-6Å or

Y is tetrazole; 1,2,3-triazole; 1,2,4-triazole; or imidazole and each of i and j is independently 0 or 1;

R⁷ is H or is ~~optionally substituted~~ alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, ~~or heteroalkyl, said heteroalkyl containing 1 or 2 O, N and/or S, or is~~ SOR, SO₂R, RCO, COOR, alkyl-COR, SO₃R, CONR₂, SO₂NR₂, CN, CF₃, NR₂, OR, alkyl-SR, alkyl-SOR, alkyl-SO₂R, alkyl-OCOR, alkyl-COOR, alkyl-CN, alkyl-CONR₂, or R₃Si, wherein each R is independently H, alkyl, alkenyl or aryl ~~or forms thereof containing 1-2 O, S and/or N atoms~~ R⁷ is methoxymethyl, methoxyethyl, ethoxymethyl, benzyloxymethyl, or 2-methoxyethyloxy methyl;

each R³ is independently ~~a noninterfering substituent~~ halo, alkyl, OCOR, OR, NRCOR, SR, or NR₂, wherein R is H, alkyl or aryl;

n is 0-3;

L¹ is CO, SO₂ or alkylene (1-4C);

L² is alkylene (1-4C) or alkenylene (2-4C) optionally substituted with one or two moieties selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, NH-aroyl, halo, OR, NR₂, SR, SOR, SO₂R, OCOR, NRCOR, NRCONR₂, NRCOOR, OCONR₂, RCO, COOR, alkyl-OOCR, SO₃R, CONR₂, SO₂NR₂, NRSO₂NR₂, CN, CF₃, and R₃Si, wherein each R is independently H, alkyl, alkenyl or aryl ~~or forms thereof containing 1-2 O, S and/or N atoms~~, and wherein two substituents on L² can be joined to form a non-aromatic saturated or unsaturated ring that includes 0-3 heteroatoms which are O, S and/or N and which contains 3 to 8 members or said two substituents can be joined to form a carbonyl moiety or an oxime, oximeether, oximeester or ketal of said carbonyl moiety;

each R^4 is independently ~~a noninterfering substituent~~ selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, NH-aroyl, halo, OR, NR_2 , SR, SOR, SO_2R , OCOR, NRCOR, $NRCONR_2$, $NRCOOR$, $OCONR_2$, RCO, COOR, alkyl-OOCR, SO_3R , $CONR_2$, SO_2NR_2 , $NRSO_2NR_2$, CN, CF_3 , R_3Si , and NO_2 , wherein each R is independently H, alkyl, alkenyl or aryl, and two of R^4 on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members, or R^4 is =O or an oxime, oximeether, oximeester or ketal thereof;

m is 0-4;

Ar is an aryl group substituted with 0-5 ~~noninterfering substituents, wherein two adjacent noninterfering substituents can form a fused ring of 3-8 members~~ substituents selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, NH-aroyl, halo, OR, NR_2 , SR, SOR, SO_2R , OCOR, NRCOR, $NRCONR_2$, $NRCOOR$, $OCONR_2$, RCO, COOR, alkyl-OOCR, SO_3R , $CONR_2$, SO_2NR_2 , $NRSO_2NR_2$, CN, CF_3 , R_3Si , and NO_2 , wherein each R is independently H, alkyl, alkenyl or aryl, and wherein two of said optional substituents on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members.

2-4. (canceled)

2 ~~5~~. (original): The compound of claim 1 wherein each of i and j is 0.

3 ~~6~~. (original): The compound of claim 2 wherein j is 0.

7-8. (canceled)

4 ~~9~~. (currently amended): The compound of claim 1 wherein R^7 is H, ~~or is optionally substituted~~ alkyl or acyl.

10-11. (canceled)

5 ~~12~~. (previously presented): The compound of claim 1 wherein L^1 is CO.

13-15. (canceled)

~~6~~ 16. (previously presented): The compound of claim 1 wherein L^2 is unsubstituted alkylene and L^1 is CO.

~~7~~ 17. (previously presented): The compound of claim 1 wherein L^2 is unsubstituted methylene, methylene substituted with alkyl, or $-CH=$ and L^1 is alkylene or CO.

18. (canceled)

~~8~~ 19. (currently amended): The compound of ~~claim 18~~ claim 1 wherein Ar is optionally substituted phenyl.

~~9~~ 20. (original): The compound of claim 19 wherein said optional substitution is by halo, OR, or alkyl.

~~10~~ 21. (original): The compound of claim 20 wherein said phenyl is unsubstituted or has a single substituent.

22. (canceled)

~~11~~ 23. (currently amended): The compound of ~~claim 22~~ claim 1 wherein each R^4 is halo, OR, or alkyl.

~~12~~ 24. (original): The compound of claim 23 wherein m is 0, 1, or 2.

~~13~~ 25. (original): The compound of claim 24 wherein m is 2 and both R^4 are alkyl.

26. (canceled)

14 27. (currently amended): The compound of ~~claim 26~~ claim 1 wherein R^3 is halo or alkoxy.

15 28. (original): The compound of claim 27 wherein n is 0, 1 or 2.

16 29. (original): The compound of claim 1 wherein L^1 is coupled to the α ring at the 4-, 5- or 6-position.

17 30. (previously presented): The compound of claim 1 wherein Z^2 at position 3 is CA or CHA.


18 31. (original): The compound of claim 30 wherein the Z^2 at position 2 is CR^1 or CR^1_2 .

32. (canceled)

19 33. (currently amended): The compound of ~~claim 32~~ claim 1 wherein each R^1 is selected from the group consisting of H, alkyl, acyl, aryl, arylalkyl, heteroaryl, halo, OR, NR_2 , SR, NRCOR, alkyl-~~OR~~ alkyl-OOCR, RCO, COOR, and CN, wherein each R is independently H, alkyl, or aryl or forms thereof containing 1-2 O, S and/or N atoms.

20 34. (original): The compound of claim 30 wherein Z^2 at position 2 is N or NR^6 .

35. (canceled)

21 36. (original): The compound of claim 1 wherein  represents a double bond.

37-38. (canceled)

61 39. (previously presented): A pharmaceutical composition for treating pathological conditions characterized by excessive p38- α activity which composition comprises a therapeutically effective amount of a compound claim 1 or the pharmaceutically acceptable salts thereof, along with a pharmaceutically acceptable excipient.

40-41. (canceled)

62 42. (previously presented): A method to treat rheumatoid arthritis comprising administering to a subject in need of such treatment a compound of claim 1 or the pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof.

43-44. (canceled)

22 45. (previously presented): The compound of claim 36, wherein Z^2 at position 3 is CA.

23 46. (previously presented): The compound of claim 45, wherein Z^2 at position 2 is CR^1 .

24 47. (previously presented): The compound of claim 46, wherein A is $COCOR^2$, wherein R^2 is as defined in claim 1.

48. (canceled)

25 49. (previously presented): The compound of claim 47, wherein R^1 is H.

26 50. (previously presented): The compound of claim 49, wherein n is 0 or 1.

27 51. (previously presented): The compound of claim 50, wherein Ar is substituted phenyl.

28 52. (previously presented): The compound of claim 51, wherein L^2 is unsubstituted or substituted alkylene.

- 29 53. (previously presented): The compound of claim 52, wherein L^1 is alkylene or CO.
- 30 54. (previously presented): The compound of claim 53, wherein L^2 is methylene and L^1 is CO.
- 31 55. (previously presented): The compound of claim 54, wherein n is 1 and R^3 is halo or methoxy.
- 32 56. (previously presented): The compound of claim 55, wherein R^7 is H or alkyl.
- 33 57. (previously presented): The compound of claim 56, wherein R^7 is methyl.
- 34 58. (previously presented): The compound of claim 57, wherein Ar is para-fluorophenyl.
- 35 59. (currently amended): The compound of claim 58, wherein R^2 is OR, NR_2 , SR, $NRCONR_2$, ONR_2 or $NRSO_2NR_2$ wherein each R is independently H, alkyl, alkenyl or aryl ~~or the forms thereof containing 1-2 O, S and/or N atoms~~ and wherein two R attached to the same N atom may form a [[3-8]] 6 membered ring selected from a morpholine ring, a piperidine ring and a piperazine ring.
- 36 60. (currently amended): The compound of claim 59, wherein R^2 is NR_2 wherein each R is independently H, alkyl, alkenyl or aryl ~~or the forms thereof containing 1-2 O, S and/or N atoms~~ and wherein two R attached to the same N atom may form a 3-8 membered ring wherein two R attached to the same N atom may form a 6 membered ring selected from a morpholine ring, a piperidine ring and a piperazine ring.
- 37 61. (previously presented): The compound of claim 60, which is selected from the group consisting of compound Nos. 15, 33, 57, 59, 77, 89, 96, and 100 of Table 2, *i.e.*,
1-methyl-6-methoxy-[4'-fluoro-(4-benzyl-2,5-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide;

1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2,5-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide;

1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide;

1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalicamide;

1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N-methyl-glyoxalicamide;

1-methyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide;

1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalic acid-morpholinamide; and

1-methyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalic acid-morpholinamide.

38 62. (previously presented): The compound of claim 60, wherein said compound is compound No. 15 of Table 2, *i.e.*, 1-methyl-6-methoxy-[4'-fluoro-(4-benzyl-2,5-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

39 63. (previously presented): The compound of claim 60, wherein said compound is compound No. 33 of Table 2, *i.e.*, 1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2,5-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

40 64. (previously presented): The compound of claim 60, wherein said compound is compound No. 57 of Table 2, *i.e.*, 1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

41 65. (previously presented): The compound of claim 60, wherein said compound is compound No. 59 of Table 2, *i.e.*, 1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalicamide.

42 66. (previously presented): The compound of claim 60, wherein said compound is compound No. 77 of Table 2, *i.e.*, 1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N-methyl-glyoxalicamide.

43 67. (previously presented): The compound of claim 60, wherein said compound is compound No. 89 of Table 2, *i.e.*, 1-methyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

44 68. (previously presented): The compound of claim 60, wherein said compound is compound No. 96 of Table 2, *i.e.*, 1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalic acid-morpholinamide.

45 69. (previously presented): The compound of claim 1, wherein said compound is compound No. 162 of Table 2, *i.e.*, 6-chloro-[4'-fluoro-(4-benzyl-2,5-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

46 70. (previously presented): The compound of claim 60, wherein said compound is compound No. 100 of Table 2, *i.e.*, 1-methyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalic acid-morpholinamide.

47 71. (previously presented): The compound of claim 1, wherein said compound is compound No. 17 of Table 2, *i.e.*, 1-ethoxycarbonyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

46 72. (previously presented): The compound of claim 1, wherein said compound is compound No. 38 of Table 2, *i.e.*, 1-ethoxycarbonyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

49 73. (previously presented): The compound of claim 1, wherein said compound is compound No. 45 of Table 2, *i.e.*, 1-t-butoxycarbonyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

50 74. (previously presented): The compound of claim 1, wherein said compound is compound No. 56 of Table 2, *i.e.*, 1-acetyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

51 75. (previously presented): The compound of claim 1, wherein said compound is compound No. 60 of Table 2, *i.e.*, 1-acetyl-2-methyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

52 76. (previously presented): The compound of claim 1, wherein said compound is compound No. 63 of Table 2, *i.e.*, 1-methoxymethyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

53 77. (previously presented): The compound of claim 1, wherein said compound is compound No. 92 of Table 2, *i.e.*, 1-methoxymethyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

54 78. (previously presented): The compound of claim 1, wherein said compound is compound No. 102 of Table 2, *i.e.*, 1-methyl-6-chloro-[4-(1-4'-fluorophenylethyl)piperazinyl]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

55 79. (previously presented): The compound of claim 1, wherein said compound is compound No. 137 of Table 3, *i.e.*, 6-methoxy-(4-benzyl piperazinyl)-indole-5-carboxamide-3-glyoxalic acid-methyl ester.

56 80. (previously presented): The compound of claim 1, wherein said compound is compound No. 138 of Table 3, *i.e.*, [4-(1-phenylethyl)piperazinyl]-indole-5-carboxamide-3-glyoxalic acid methyl ester.

57 81. (previously presented): The compound of claim 1, wherein said compound is compound No. 152 of Table 3, *i.e.*, (4-benzyl-2R,5S-piperazinyl)-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

58 82. (previously presented): The compound of claim 1, wherein said compound is compound No. 161 of Table 3, *i.e.*, 6-methoxy-[4'-fluoro-(4-benzyl-2,5-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalic acid-morpholinamide.

59 83. (previously presented): The compound of claim 1, wherein said compound is compound No. 177 of Table 3, *i.e.*, 6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

60 84. (previously presented): The compound of claim 1, wherein said compound is compound No. 180 of Table 3, *i.e.*, (6-methoxy[4-(1-4'-fluorophenylethyl)piperazinyl]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.